

- D. J. C.*
- a) removing cell debris from the digested cells by passing the digested cells through a filter having decreasing filter pore size in flow direction to effect an effluent, and
 - b) applying the effluent to a mineral support in a buffer solution of high ionic strength.
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REMARKS

The present claims are 40-59, which correspond to cancelled claims 1-33 and 35-38, rewritten in order to more clearly define the present invention.

Matters concerning the restriction requirement, "use" claims, and multiple dependency are rendered moot since the present amendment cancels the non-elected claims.

Claims were rejected under 35 U.S.C. §112, second paragraph. Reconsideration is respectfully requested in view of the present amendment, which rewrites the claims in more typical U.S. format.

Claims stand rejected under 35 U.S.C. §103, as being allegedly unpatentable based on Hagen, Sternberg, Henco, Riesner, Little, and Schneider. Reconsideration is respectfully requested.

Henco is the U.S. patent that corresponds to EP-A-0 268 946, which was discussed during the international examination procedure. The international examination authority (IPEA) concluded that Henco is the closest state of the art and that the subject matter of the present application is patentable over that reference (cf. translation of the international preliminary

examination report is enclosed herewith). While, certainly, not bound by the conclusion of the international authority, the examiner is respectfully requested to consider the IPEA report.

The report states that the method claimed in the present application does not follow obviously from the closest state of the art, which is Henco. Thus, an inventive step (unobviousness) was acknowledged in view of Henco.

Hagen was also cited in the international search report, as well as Sternberg. Hagen deals with a composite chromatographic article comprising a polytetrafluoroethylene fibril matrix and non-swellable sorptive particles enmeshed in said matrix. The ratio of non-swellable sorptive particles to polytetrafluoroethylene is in the range of 19:1 to 4:1, by weight. The composite article has a net surface energy in the range of 20 to 300 milliNewtons per meters.

Hagen neither teaches nor suggests the combination of process steps presently claimed. Nothing in the references suggests to the skilled person to, first, adsorb nucleic acids on a matrix, ("subjecting ... to anion exchange"), under conditions of low ionic strength, and, then, elute the nucleic acids from the matrix, with a buffer of "ionic strength higher than the first adsorption buffer," bind that higher ionic strength medium onto a solid support by using a "buffer having an ionic strength lower than the second buffer." The skilled person derives no motivation to even think about such a second adsorption step. Therefore,

Henco would never suggest the presently claimed process to the art-skilled person.

Sternberg is only concerned with an apparatus that is a membrane unit, which can sealably accommodate a variable number of stacked, planar membrane (sheet filter) elements. The different sheet filter elements may be modified by different biological materials, such as antigens, monoclonal antibodies, and so on. Nothing, whatsoever, can the skilled person derive with respect to a process using the buffer solution as recited in the present claims. Also, there is no motivation to combine that reference with other references cited by the Examiner.

Little deals with a process for the purification of plasmids and other DNA, both single-stranded and double-stranded. The process involves immobilizing the DNA onto diatomaceous earth in the presence of a chaotropic agent and eluting the DNA with water or low-salt buffer. The resulting purified DNA is biologically active. Also, included in that disclosure is a process for the immobilization of DNA onto diatomaceous earth in the presence of a chaotropic agent.

However, Little is particularly silent with respect to the preparation of nucleic acids via anion exchange purification. On the contrary, the advantage of anion exchange is that, directly from cell lysis, the respective samples can be taken and further processed. Therefore, this reference more teaches away from, than suggests, the process steps claimed in the present invention.

Little just discloses the use of a chaotropic salt of high ionic strength.

Riesner merely teaches, in isolation, nucleic-acid separation using anion exchange chromatography. Nothing in the reference suggests any other nucleic-acid processing, either before or after anion exchange.

The presently claimed invention differs in a non-obvious manner from the cited prior art since neither Henco nor Riesner elute with a salt, generally, or chaotropic salt, in particular, of high ionic strength, even in view of Little. It is well known to the skilled person that elution from an anionic exchanger takes place in a concentration of about 1.5 M sodium chloride as the highest concentration. On other hand, binding on Little's matrix does not occur with any sodium chloride concentration since sodium chloride is not a chaotropic salt, which Little requires. Binding of nucleic acids on a matrix according to Little can only be achieved with (i) chaotropic salts and (ii) in high concentrations corresponding to about 6 M NaClO₄.

There was not motivation to combine the references cited by the examiner other than provoked with the wisdom of hindsight. Since the references cited had different objectives, which partially do not have anything to do with the objective to be solved by the present invention, the skilled person would not combine the references, as suggested by the examiner. Even if the artisan would combine all the references, or some of the

references, it would not effect the process of the present invention as claimed.

The object of the present invention was to provide a process enabling isolation and purification of nucleic acids, without the requirement of a centrifugation step to remove cell fragments or undissolved components. For example, this object was not addressed by Little.

Similarly, the criticism of original claims 35 and 37 is not justified even if the filtration or the adsorption step in presence of high ionic strength were not recited. The skilled person would not have received any motivation to combine the references in order to end up with the steps recited in original claims 35 and 37.

With all due respect, picking and choosing from among the cited references various elements in order to fashion the presently claimed process is the result of hindsight reconstruction, rather than a combination that one of ordinary skill in the art had been motivated to effect. The only motivation of record is that the presently claimed invention

is a combination of process steps well known in the art and motivated by the disclosures of Henco et al. '426, Riesner et al. '727, and Little '430. The use of a specific filtration methodology (i.e. variation in filter porosity) such as those taught by Hagen et al. '381 or Sternberg '142 is deemed to be incorporation of a variation clearly within the purview of the ordinary practitioner seeking to optimize the result of the Henco methodology.

The examiner argues that the combination would have been "motivated by the disclosures" of the cited references, with no foundation established as to what the alleged motivation is or where the alleged motivation is to be found in the cited references. Obviousness is not established by making "unfounded assumptions or hindsight reconstruction to supply deficiencies in the factual basis." In re Warner, 154 USPQ 173, 178 (CCPA 1967).

The examiner argues, with insufficient factual basis, that combining the references is "deemed" to have been obvious to one trying to optimize the teachings of Henco.

The examiner should be aware that "deeming" does not discharge him from the burden of providing a requisite factual basis and establishing the requisite motivation to support the conclusion of obviousness.

Ex parte Stern, 13 USPQ 2d 1379, 1381 (BPAI 1989). With respect to the "variation" allegedly optimizing the results of Henco, if the prior art fails to disclose a rationale for varying parameters to be result-effective, it cannot have been obvious to chose the claimed parameter. In re Antonie, 195 USPQ 6 (CCPA 1977).

Finally, the examiner concludes that "said subject matter is found to include no adequate basis for a finding of patentability in view of the noted prior art." With all due respect, applicants submit that the quoted statement evidences a misconception of a proper patentability analysis, which could have affected the manner in which the analysis was conducted in the present case.

The PTO is charged with determining whether a claimed invention is not patentable based on the prior art. It is, accordingly, improper to approach the prior art with a view toward determining an "adequate basis for a finding of patentability" (emphasis added). The notion of examination by looking for something to establish patentability was long ago rejected as a proper way of conducting a patentability analysis. Graham v. John Deere Co., 383 U.S. 1 (1966). It is improper to look for a particular claim limitation and determine whether such a limitation provides an "adequate basis for a finding of patentability." The PTO must examine the claims as a whole and determine the differences between the claimed invention and the prior art and, then, determine whether the prior art in combination with those differences would have been obvious, not whether the differences are an "adequate basis for a finding of patentability." Id.

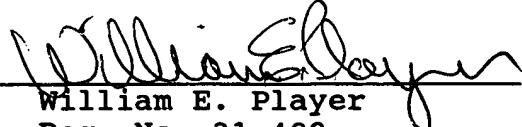
Accordingly, for the foregoing reasons, the present claims are considered allowable and a favorable action is requested.

Favorable action commensurate with the foregoing is requested.

Respectfully submitted,

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